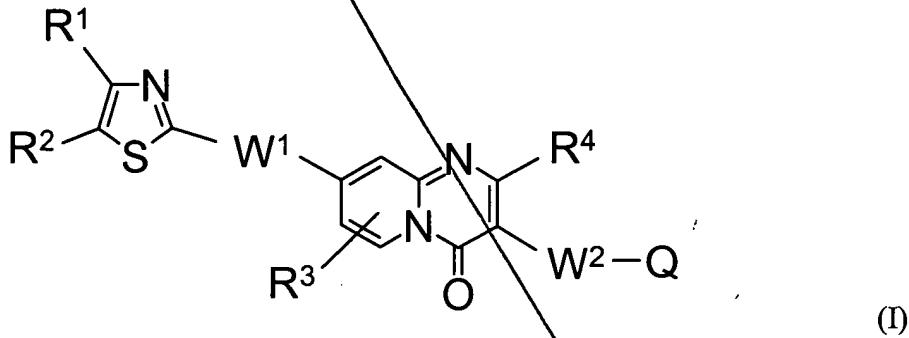


IN THE CLAIMS

Please cancel claims 19, 21 and 23 without prejudice or disclaimer of the subject matter recited therein, and reserving the right to file one or more continuing applications directed to the canceled subject matter.

Please amend claims 1, 5, 12, 18 and 25 as follows, with marked up copies of the claims being included in an Appendix attached hereto:

1. (Twice Amended) A compound represented by the following formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof:



wherein, R¹ and R² each independently represent hydrogen atom, a halogen atom, hydroxyl group, a group of OZ₁₋₆ (the group of OZ₁₋₆ represents an alkyl group having 1-6 carbon atoms or a fluoroalkyl group having 1-6 carbon atoms, which bonds via the oxygen atom), a group of S(O)_nZ₁₋₄ (Z₁₋₄ represents an alkyl group having 1-4 carbon atoms or a fluoroalkyl group having 1-4 carbon atoms or an alkylene group derived therefrom), a group of N(R¹²)(R¹³) (R¹² and R¹³

each independently represent hydrogen atom, an alkyl group having 1-4 carbon atoms or a fluoroalkyl group having 1-4 carbon atoms), a group of Z_{1-8} which may be substituted (Z_{1-8} represents an alkyl group having 1-8 carbon atoms or a fluoroalkyl group having 1-8 carbon atoms), a 5- to 7-membered cyclic alkyl group, an aryl group, a heteroaryl group, or a 4- to 7-membered saturated or partially saturated heterocyclic group (the cyclic alkyl group, aryl group, heteroaryl group and heterocyclic group may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of OZ_{1-4} , a group of $S(O)_nZ_{1-4}$, a group of $N(R^{12})(R^{13})$, a group of Z_{1-4} , carboxyl group, a group of CO_2Z_{1-4} , group of $CONH_2$, a group of $CONH(Z_{1-4})$ and a group of $CON(Z_{1-4})(Z_{1-4})$);

W^1 represents a group selected from the group consisting of $-CH=CH-$, $-N(R^{12})CO-$, $-CON(R^{12})-$, $-CH_2O-$ and $-CH_2CH_2-$ (each of the aforementioned groups binds to the thiazole ring at the left end);

R^3 represents hydrogen atom, a halogen atom, hydroxyl group or an amino group;

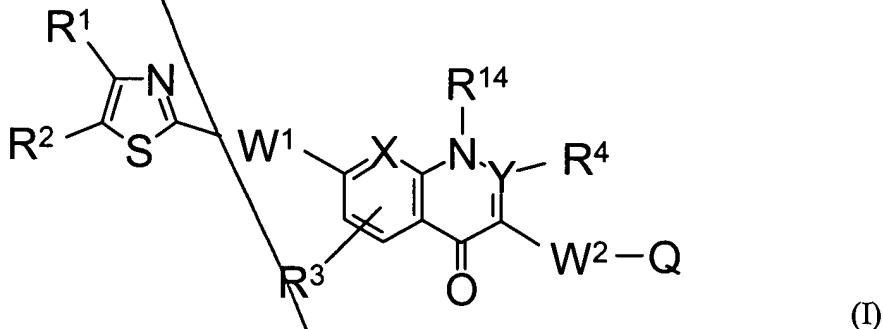
R^4 represents a group selected from the group consisting of hydrogen atom, a group of $-OZ_{0-4}R^5$ (Z_{0-4} represents an alkylene group having 1-4 carbon atoms, a fluorine-substituted alkylene group having 1-4 carbon atoms or a single bond, and R^5 represents a 5- to 7-membered cyclic alkyl group, an aryl group, a heteroaryl group or a 4- to 7-membered saturated or partially saturated heterocyclic group (the cyclic alkyl group, aryl group, heteroaryl group and heterocyclic group may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of OZ_{1-4} , a group of $S(O)_nZ_{1-4}$, a group of $N(R^{12})(R^{13})$, a group of Z_{1-4} , carboxyl group, a group of CO_2Z_{1-4} , group of $CONH_2$, a group of $CONH(Z_{1-4})$ and a group of

~~CON(Z₁₋₄)(Z₁₋₄)), a group of -S(O)_nZ₀₋₄R⁵, a group of -N(R⁶)(R⁷) {R⁶ and R⁷ each independently represent hydrogen atom or Z₁₋₄, or they may bind to each other to form a saturated or unsaturated 5- to 7-membered ring (the ring may contain one or two hetero atoms as ring constituting atoms), and R⁶ and R⁷ may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of OCON(R¹²)(R¹³), a group of CON(R¹²)(R¹³), a group of N(R¹²)CON(R¹²)(R¹³), a group of Z₁₋₄, a group of OZ₁₋₄, a group S(O)_nZ₁₋₄, group of CH₂OH, a group of (CH₂)_mN(R¹²)(R¹³), carboxyl group, cyano group, a group of CO-Z₁₋₄(R¹⁰)-N(R¹²)(R¹³) (R¹⁰ is a substituent corresponding to a side chain on an amino acid carbon or a group of -Z₁₋₄-R¹¹ (R¹¹ represents a substituent which forms a quaternary salt) and a~~

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group of $\text{CO} \cdot \underset{\substack{| \\ (\text{CH}_2)^q}}{\text{Z}_{1-4}} \cdot \text{N}(\text{R}^{12})(\text{R}^{13})$ }, a 5- or 6-membered aryl group which may be substituted and a 5- or 6-membered unsaturated heterocyclic group which may be substituted;

W² represents a single bond or -C(R⁸)=C(R⁹)- (R⁸ and R⁹ each independently represent hydrogen atom, a halogen atom, a lower alkyl group, an alkoxy group, cyano group, carboxyl group, hydroxymethyl group, cyanomethyl group, vinyl group or a group of N(R¹²)(R¹³)), Q represents an acidic group, and W² and Q may bind together to form vinylidenethiazolidinedione in *E*- or *Z*-configuration or an equivalent heterocyclic ring; m and n each independently represent an integer of 0 to 2, and q represents an integer of 0 to 3.

C2
5. (Twice Amended) A compound represented by the following formula (I) or a physiologically acceptable salt thereof, or hydrate thereof



Sub 101
wherein, R¹ and R² each independently represent hydrogen atom, a halogen atom, hydroxyl group, a group of OZ₁₋₆ (the group of OZ₁₋₆ represents an alkyl group having 1-6 carbon atoms or a fluoroalkyl group having 1-6 carbon atoms, which bonds via the oxygen atom), a group of S(O)_nZ₁₋₄ (Z₁₋₄ represents an alkyl group having 1-4 carbon atoms or a fluoroalkyl group having 1-4 carbon atoms or an alkylene group derived therefrom), a group of N(R¹²)(R¹³) (R¹² and R¹³ each independently represent hydrogen atom, an alkyl group having 1-4 carbon atoms or a fluoroalkyl group having 1-4 carbon atoms), a group of Z₁₋₈ which may be substituted (Z₁₋₈ represents an alkyl group having 1-8 carbon atoms or a fluoroalkyl group having 1-8 carbon atoms), a 5- to 7-membered cyclic alkyl group, an aryl group, a heteroaryl group, or a 4- to 7-membered saturated or partially saturated heterocyclic group (the cyclic alkyl group, aryl group, heteroaryl group and heterocyclic group may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of OZ₁₋₄, a group of S(O)_nZ₁₋₄, a group of N(R¹²)(R¹³), a group of Z₁₋₄, carboxyl group, a group of CO₂Z₁₋₄, group of CONH₂, a group of CONH(Z₁₋₄) and a group of CON(Z₁₋₄)(Z₁₋₄));

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W^1 represents a group selected from the group consisting of $-\text{CH}=\text{CH}-$, $-\text{N}(\text{R}^{12})\text{CO}-$, $-\text{CON}(\text{R}^{12})-$, $-\text{CH}_2\text{O}-$ and $-\text{CH}_2\text{CH}_2-$ (each of the aforementioned groups binds to the thiazole ring at the left end);

R^3 represents hydrogen atom, a halogen atom, hydroxyl group or an amino group;

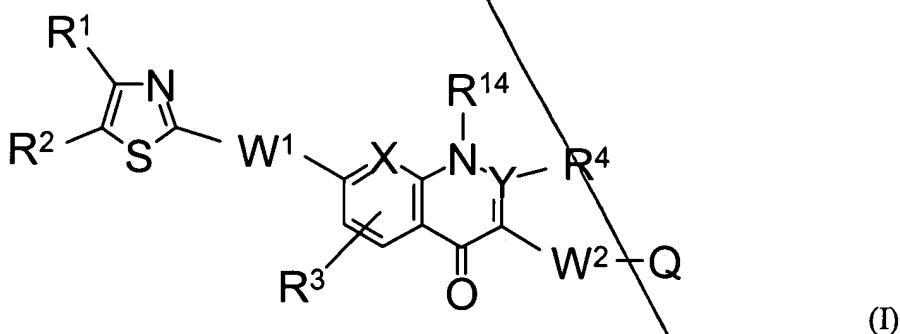
R^4 represents a group selected from the group consisting of hydrogen atom, a group of $-\text{OZ}_{0.4}\text{R}^5$ ($Z_{0.4}$ represents an alkylene group having 1-4 carbon atoms, a fluorine-substituted alkylene group having 1-4 carbon atoms or a single bond, and R^5 represents a 5- to 7-membered cyclic alkyl group, an aryl group, a heteroaryl group or a 4- to 7-membered saturated or partially saturated heterocyclic group (the cyclic alkyl group, aryl group, heteroaryl group and heterocyclic group may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of $\text{OZ}_{1.4}$, a group of $\text{S}(\text{O})_n\text{Z}_{1.4}$, a group of $\text{N}(\text{R}^{12})(\text{R}^{13})$, a group of $\text{Z}_{1.4}$, carboxyl group, a group of $\text{CO}_2\text{Z}_{1.4}$, group of CONH_2 , a group of $\text{CONH}(\text{Z}_{1.4})$ and a group of $\text{CON}(\text{Z}_{1.4})(\text{Z}_{1.4})$), a group of $-\text{S}(\text{O})_n\text{Z}_{0.4}\text{R}^5$, a group of $-\text{N}(\text{R}^6)(\text{R}^7)$ { R^6 and R^7 each independently represent hydrogen atom or $Z_{1.4}$, or they may bind to each other to form a saturated or unsaturated 5- to 7-membered ring (the ring may contain one or two hetero atoms as ring constituting atoms), and R^6 and R^7 may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of $\text{OCON}(\text{R}^{12})(\text{R}^{13})$, a group of $\text{CON}(\text{R}^{12})(\text{R}^{13})$, a group of $\text{N}(\text{R}^{12})\text{CON}(\text{R}^{12})(\text{R}^{13})$, a group of $\text{Z}_{1.4}$, a group of $\text{OZ}_{1.4}$, a group of $\text{S}(\text{O})_n\text{Z}_{1.4}$, group of CH_2OH , a group of $(\text{CH}_2)_m\text{N}(\text{R}^{12})(\text{R}^{13})$, carboxyl group, cyano group, a group of $\text{CO-Z}_{1.4}(\text{R}^{10})-\text{N}(\text{R}^{12})(\text{R}^{13})$ (R^{10} is a substituent corresponding to a side chain on an amino acid carbon or a group of $-\text{Z}_{1.4}-\text{R}^{11}$ (R^{11} represents a substituent which forms a quaternary salt) and a

group of $\text{CO} \cdot \text{Z}_{1-4} \cdot \text{N}(\text{R}^{12})(\text{R}^{13})$
 $(\text{CH}_2)^q$ }, a 5- or 6-membered aryl group which may be substituted and a 5-
or 6-membered unsaturated heterocyclic group which may be substituted;
 W^2 represents a single bond or $-\text{C}(\text{R}^8)=\text{C}(\text{R}^9)-$ (R^8 and R^9 each independently represent hydrogen
atom, a halogen atom, a lower alkyl group, an alkoxy group, cyano group, carboxyl group,
hydroxymethyl group, cyanomethyl group, vinyl group or a group of $\text{N}(\text{R}^{12})(\text{R}^{13})$), Q represents
an acidic group, and W^2 and Q may bind together to form vinylidenethiazolidinedione in *E*- or *Z*-
configuration or an equivalent heterocyclic ring; m and n each independently represent an integer
of 0 to 2, and q represents an integer of 0 to 3; R^{14} represents hydrogen atom, Z_{1-4} , Z_{1-4}R^5 or
 $\text{Z}_{1-4}\text{OR}^5$; and X represents C-H and Y represents C-H or nitrogen atom.

12. (Amended) The method according to claim 7 wherein mammal is a human.

18. (Amended) The method according to claim 13 wherein the mammal is a human.

25. (Amended) A method for therapeutic treatment of a microbial infection comprising administering to a mammal in need thereof a therapeutically effective amount of a composition comprising a compound represented by formula (I) or a physiologically acceptable salt thereof as an active ingredient and at least one antimicrobial agent



wherein R¹ and R² each independently represent hydrogen atom, a halogen atom, hydroxyl group, a group of OZ₁₋₆ (the group of OZ₁₋₆ represents an alkyl group having 1-6 carbon atoms or a fluoroalkyl group having 1-6 carbon atoms, which bonds via the oxygen atom), a group of S(O)_nZ₁₋₄ (Z₁₋₄ represents an alkyl group having 1-4 carbon atoms or a fluoroalkyl group having 1-4 carbon atoms or an alkylene group derived therefrom), a group of N(R¹²)(R¹³) (R¹² and R¹³ each independently represent hydrogen atom, an alkyl group having 1-4 carbon atoms or a fluoroalkyl group having 1-4 carbon atoms), a group of Z₁₋₈ which may be substituted (Z₁₋₈ represents an alkyl group having 1-8 carbon atoms or a fluoroalkyl group having 1-8 carbon atoms), a 5- to 7-membered cyclic alkyl group, an aryl group, a heteroaryl group, or a 4- to 7-membered saturated or partially saturated heterocyclic group (the cyclic alkyl group, aryl group, heteroaryl group and heterocyclic group may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of OZ₁₋₄, a group of S(O)_nZ₁₋₄, a group of N(R¹²)(R¹³), a group of Z₁₋₄, carboxyl group, a group of CO₂Z₁₋₄, group of CONH₂, a group of CONH(Z₁₋₄) and a group of CON(Z₁₋₄)(Z₁₋₄));

W¹ represents a group selected from the group consisting of -CH=CH-, -N(R¹²)CO-, -CON(R¹²)-, -CH₂O- and -CH₂CH₂- (each of the aforementioned groups binds to the thiazole ring at the left end);

R³ represents hydrogen atom, a halogen atom, hydroxyl group or an amino group;

R⁴ represents a group selected from the group consisting of hydrogen atom, a group of -OZ₀₋₄R⁵ (Z₀₋₄ represents an alkylene group having 1-4 carbon atoms, a fluorine-substituted alkylene group having 1-4 carbon atoms or a single bond, and R⁵ represents a 5- to 7-membered cyclic alkyl

group, an aryl group, a heteroaryl group or a 4- to 7-membered saturated or partially saturated heterocyclic group (the cyclic alkyl group, aryl group, heteroaryl group and heterocyclic group may have one to three substituents selected from the group consisting of a halogen atom,

C5
C6H

hydroxyl group, a group of OZ_{1-4} , a group of $S(O)_nZ_{1-4}$, a group of $N(R^{12})(R^{13})$, a group of Z_{1-4} , carboxyl group, a group of CO_2Z_{1-4} , group of $CONH_2$, a group of $CONH(Z_{1-4})$ and a group of $CON(Z_{1-4})(Z_{1-4})$, a group of $-S(O)_nZ_{0-4}R^5$, a group of $-N(R^6)(R^7)$ { R^6 and R^7 each independently represent hydrogen atom or Z_{1-4} , or they may bind to each other to form a saturated or unsaturated 5- to 7-membered ring (the ring may contain one or two hetero atoms as ring constituting atoms), and R^6 and R^7 may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of $OCON(R^{12})(R^{13})$, a group of $CON(R^{12})(R^{13})$, a group of $N(R^{12})CON(R^{12})(R^{13})$, a group of Z_{1-4} , a group of OZ_{1-4} , a group of $S(O)_nZ_{1-4}$, group of CH_2OH , a group of $(CH_2)_mN(R^{12})(R^{13})$, carboxyl group, cyano group, a group of $CO-Z_{1-4}(R^{10})-N(R^{12})(R^{13})$ (R^{10} is a substituent corresponding to a side chain on an amino acid carbon or a group of $-Z_{1-4}R^{11}$ (R^{11} represents a substituent which forms a quaternary salt) and a

group of $\begin{array}{c} CO \cdot Z_{1-4} \cdot N(R^{12})(R^{13}) \\ | \\ (CH_2)^q \end{array} \}$, a 5- or 6-membered aryl group which may be substituted and a 5- or 6-membered unsaturated heterocyclic group which may be substituted;

W^2 represents a single bond or $-C(R^8)=C(R^9)-$ (R^8 and R^9 each independently represent hydrogen atom, a halogen atom, a lower alkyl group, an alkoxy group, cyano group, carboxyl group, hydroxymethyl group, cyanomethyl group, vinyl group or a group of $N(R^{12})(R^{13})$), Q represents an acidic group, and W^2 and Q may bind together to form vinylidenethiazolidinedione in *E*- or *Z*-

*C5
C-H
Cont*

configuration or an equivalent heterocyclic ring; m and n each independently represent an integer of 0 to 2, and q represents an integer of 0 to 3; R¹⁴ represents hydrogen atom, an alkyl group having 1, 3 or 4 carbon atoms or a fluoroalkyl group having 1-4 carbon atoms, Z₁₋₄R⁵ or Z₁₋₄OR⁵; and X and Y each independently represent C-H or nitrogen atom.

C6

Please add claims 28-33, as follows:

28. (New) A method for inhibiting drug resistance acquisition due to a drug efflux pump comprising administering to a mammal an effective amount to inhibit drug resistance acquisition due to a drug efflux pump of the composition according to claim 6.

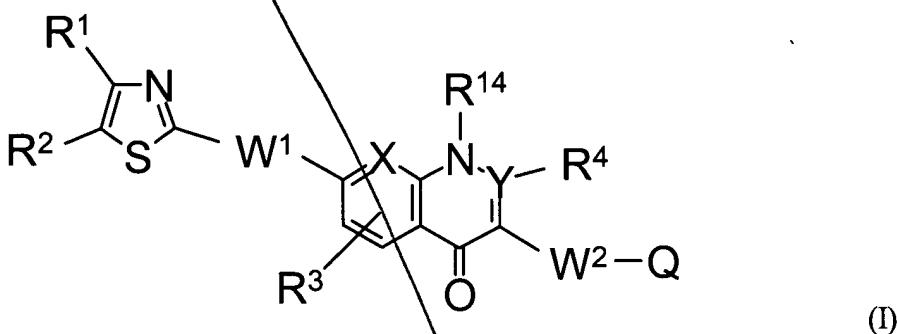
29. (New) The method according to claim 28 wherein the mammal is a human.

30. (New) A method for inhibiting drug resistance acquisition due to a drug efflux pump comprising administering to a mammal an effective amount to inhibit drug resistance acquisition due to a drug efflux pump of the composition according to claim 20.

31. (New) The method according to claim 30 wherein the mammal is a human.

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32. (New) A method for inhibiting drug resistance acquisition due to a drug efflux pump comprising administering to a mammal an effective amount to inhibit drug resistance acquisition due to a drug efflux pump of a composition comprising a compound represented by formula (I) or a physiologically acceptable salt thereof as an active ingredient



wherein, R¹ and R² each independently represent hydrogen atom, a halogen atom, hydroxyl group, a group of OZ₁₋₆ (the group of OZ₁₋₆ represents an alkyl group having 1-6 carbon atoms or a fluoroalkyl group having 1-6 carbon atoms, which bonds via the oxygen atom), a group of S(O)_nZ₁₋₄ (Z₁₋₄ represents an alkyl group having 1-4 carbon atoms or a fluoroalkyl group having 1-4 carbon atoms or an alkylene group derived therefrom), a group of N(R¹²)(R¹³) (R¹² and R¹³ each independently represent hydrogen atom, an alkyl group having 1-4 carbon atoms or a fluoroalkyl group having 1-4 carbon atoms), a group of Z₁₋₈ which may be substituted (Z₁₋₈ represents an alkyl group having 1-8 carbon atoms or a fluoroalkyl group having 1-8 carbon atoms), a 5- to 7-membered cyclic alkyl group, an aryl group, a heteroaryl group, or a 4- to 7-membered saturated or partially saturated heterocyclic group (the cyclic alkyl group, aryl group, heteroaryl group and heterocyclic group may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of OZ₁₋₄, a group of S(O)_nZ₁₋₄, a

group of $N(R^{12})(R^{13})$, a group of Z_{1-4} , carboxyl group, a group of CO_2Z_{1-4} , group of $CONH_2$, a group of $CONH(Z_{1-4})$ and a group of $CON(Z_{1-4})(Z_{1-4})$);

W^1 represents a group selected from the group consisting of $-CH=CH-$, $-N(R^{12})CO-$, $-CON(R^{12})-$, $-CH_2O-$ and $-CH_2CH_2-$ (each of the aforementioned groups binds to the thiazole ring at the left end);

R^3 represents hydrogen atom, a halogen atom, hydroxyl group or an amino group;

R^4 represents a group selected from the group consisting of hydrogen atom, a group of $-OZ_{0-4}R^5$ (Z_{0-4} represents an alkylene group having 1-4 carbon atoms, a fluorine-substituted alkylene group having 1-4 carbon atoms or a single bond, and R^5 represents a 5- to 7-membered cyclic alkyl group, an aryl group, a heteroaryl group or a 4- to 7-membered saturated or partially saturated heterocyclic group (the cyclic alkyl group, aryl group, heteroaryl group and heterocyclic group may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of OZ_{1-4} , a group of $S(O)_nZ_{1-4}$, a group of $N(R^{12})(R^{13})$, a group of Z_{1-4} , carboxyl group, a group of CO_2Z_{1-4} , group of $CONH_2$, a group of $CONH(Z_{1-4})$ and a group of $CON(Z_{1-4})(Z_{1-4})$), a group of $-S(O)_nZ_{0-4}R^5$, a group of $-N(R^6)(R^7)$ { R^6 and R^7 each independently represent hydrogen atom or Z_{1-4} , or they may bind to each other to form a saturated or unsaturated 5- to 7-membered ring (the ring may contain one or two hetero atoms as ring constituting atoms), and R^6 and R^7 may have one to three substituents selected from the group consisting of a halogen atom, hydroxyl group, a group of $OCON(R^{12})(R^{13})$, a group of $CON(R^{12})(R^{13})$, a group of $N(R^{12})CON(R^{12})(R^{13})$, a group of Z_{1-4} , a group of OZ_{1-4} , a group of $S(O)_nZ_{1-4}$, group of CH_2OH , a group of $(CH_2)_mN(R^{12})(R^{13})$, carboxyl group, cyano group, a group

of $\text{CO-Z}_{1-4}(\text{R}^{10})-\text{N}(\text{R}^{12})(\text{R}^{13})$ (R^{10} is a substituent corresponding to a side chain on an amino acid carbon or a group of $\text{Z}_{1-4}-\text{R}^{11}$ (R^{11} represents a substituent which forms a quaternary salt) and a

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group of $\text{CO-Z}_{1-4}-\text{N}(\text{R}^{12})(\text{R}^{13})$
 $(\text{CH}_2)_q$, a 5- or 6-membered aryl group which may be substituted and a 5-
 or 6-membered unsaturated heterocyclic group which may be substituted;

W^2 represents a single bond or $-\text{C}(\text{R}^8)=\text{C}(\text{R}^9)-$ (R^8 and R^9 each independently represent hydrogen atom, a halogen atom, a lower alkyl group, an alkoxy group, cyano group, carboxyl group, hydroxymethyl group, cyanomethyl group, vinyl group or a group of $\text{N}(\text{R}^{12})(\text{R}^{13})$), Q represents an acidic group, and W^2 and Q may bind together to form vinylidenethiazolidinedione in *E*- or *Z*-configuration or an equivalent heterocyclic ring; m and n each independently represent an integer of 0 to 2, and q represents an integer of 0 to 3; R^{14} represents hydrogen atom, an alkyl group having 1, 3 or 4 carbon atoms or a fluoroalkyl group having 1-4 carbon atoms, Z_{1-4}R^5 or $\text{Z}_{1-4}\text{OR}^5$; and X and Y each independently represent C-H or nitrogen atom.

33. (New) The method according to claim 32 wherein the mammal is a human.

REMARKS

Upon entry of the instant amendment, claims 19, 21 and 23 will be canceled without prejudice or disclaimer, claims 1, 5, 12, 18 and 25 will be amended, and claims 28-33 will be added, whereby claims 1-33 will be pending. Claims 1, 5 and 19 are independent claims.

Claims 1, 5 and 25 have been amended to even more clearly denote formula (I), claims 12 and 18 have been amended to clarify the claim language by inserting "the" before "mammal",